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Topical Pharmacotherapy for Allergic Rhinitis: Nedocromil

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The management of nasal allergy by pharmacotherapy is a major part of the practice of otolaryngologists and allergists as well as primary care physicians. The use of topical preparations for this purpose has become increasingly popular, as new and better drugs of several types continue to be introduced.¹

Topical cromolyn is used in the treatment of mild to moderate allergic rhinitis, exerting both a protective and therapeutic effect by stabilizing mast cells against degranulation. Corticosteroids have a potent antiinflammatory action and are frequently used to treat moderate to severe rhinitis. Topical corticosteroid use has continued to increase following the introduction of beclomethasone in the 1970s, and new preparations are becoming available with increasing frequency. Other than cromolyn, no mast-cell stabilizers had been introduced until the development of nedocromil. Nedocromil is more potent than cromolyn and combines mast-cell stabilization properties with a broad antiinflammatory action that affects the inflammatory response at several sites. Like cromolyn, nedocromil inhibits both the immediate and late phases of the allergic reaction.

CHARACTERISTICS

Nedocromil sodium is the disodium salt of a pyranoquinoline dicarboxylic acid. It stabilizes both mucosal and connective tissue mast cells as well as eosinophils, monocytes, epi-

thelial cells, and alveolar macrophages. The mucosal mast-cell stabilizing potency of nedocromil has been determined to be at least 100 times that of cromolyn sodium.² Also, biopsy studies of nasal mucous membrane have shown that treatment with nedocromil sodium significantly inhibits the accumulation of mast cells within the tissue.³ In addition, nedocromil appears to suppress the action or formation of multiple mediators, including histamine, leukotriene C₄, and prostaglandin D₂.⁴ Although statistical comparison is difficult, it appears by clinical assessment that nedocromil is significantly more potent for the treatment of allergic rhinitis than cromolyn.⁵

NEDOCROMIL FOR ALLERGIC RHINITIS

Nedocromil is administered topically into the nose as a 1% solution dispensed by a pump spray. As is the case with cromolyn, pretreatment of nasal mucosa with topical nedocromil before an allergen challenge significantly reduces such effects as nasal obstruction, rhinorrhea, and sneezing.⁶

In addition to this protective effect, intranasal nedocromil administered 2 to 4 times daily to ragweed-allergic patients during ragweed season has been shown to significantly reduce sneezing, rhinorrhea, itching membranes, nasal congestion, sleep disturbances due to allergic symptoms, and the requirement for concomitant medications.⁷⁻⁹ A similar beneficial effect has been demonstrated in a double-blind, placebo-controlled study in which nedocromil was administered to patients with grass allergy during peak pollen season.¹⁰

Nedocromil combined with astemizole has been demonstrated to be much more effective than the antihistamine alone in relieving allergic rhinitis symptoms.¹¹

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PROPER USE

To be effective, intranasal nedocromil must be widely dispersed over the involved area.¹² This may require an initial concomitant administration of a decongestant or the use of a saline nasal spray to flush thick secretions from the nose before nedocromil spray is administered. Nedocromil, like cromolyn, is ineffective in the treatment of polyps.¹³ Other than its application before an anticipated acute allergen exposure, nedocromil cannot be used on an as-needed basis. Rather, to adequately control the symptoms of mild to moderate allergic rhinitis, nedocromil must be used regularly throughout the patient's usual allergic season. However, clinical experience indicates that once effective symptom control has been achieved with the 4 times daily dosage, the maintenance dose may be decreased to a frequency of 2 times daily.

SIDE EFFECTS AND SAFETY

Nedocromil has an exceptional safety profile with a low incidence of reported side effects that are generally mild. These have consisted primarily of nasal dryness and stinging, in about the same proportion (or less) as observed in patients receiving placebo.^{7,8} No constitutional symptoms attributable to topically administered nedocromil have been reported in the references reviewed.

OTHER USES OF INTRANASAL NEDOCROMIL

Although not approved for such use, many physicians have found through clinical experience that topical application of cromolyn will effectively protect many patients from nasal symptoms produced by nonimmunologic triggers (eg, irritant fumes). Insufficient experience has been gathered with nedocromil to judge whether it will also be effective in these situations. However, its unique dual action of mast-cell stabilization and antiinflammatory action makes it likely that such use would be appropriate. In inhalational challenge studies in asthma, nedocromil is consistently more potent than cromolyn sodium against nonim-

munologic challenges such as sulfur dioxide or sulfites.¹⁴

In a placebo-controlled study, administration of intranasal nedocromil to volunteers infected with rhinovirus significantly lowered both their daily symptom scores and daily mean nasal secretions.¹⁵ In a group infected with coronavirus, no statistically significant difference in the two groups was demonstrable, although clinical indicators favored the nedocromil group. In both groups (rhinovirus and coronavirus), nedocromil administration improved the symptoms of the infected individuals. The authors concluded that one or more of the mediators affected by nedocromil was involved in the production of symptoms by these viral respiratory infections.

NEDOCROMIL FOR LOWER AIRWAY USE

The only form of nedocromil currently available in the United States for pulmonary administration is an inhalational aerosol delivered via a metered dose inhaler (Tilade, Fisons Corporation, Rochester, NY). Studies have shown it to be both a safe and effective first-line agent in the preventive management of asthma, whether allergic or nonallergic.¹⁶⁻¹⁸ In general, nedocromil is believed to be as potent and safe for first-line maintenance therapy in mild to moderate asthma in adults as cromolyn has proven to be in pediatrics. As with the nasal solution, initial dosing is at a frequency of 4 times daily. However, it is generally possible to maintain adequate asthma control with a twice-daily regimen.

SUMMARY

Nedocromil sodium is a mast-cell stabilizer that prevents or ablates both the acute and late phases of the allergic response. It is an antiinflammatory agent that is not a steroid. It is more potent than the currently available mast-cell stabilizer, cromolyn, and maintenance therapy may be possible at less frequent intervals than the initially recommended regimen of 4 times daily. Nedocromil for pulmonary administration is currently available. The nasal form has undergone clinical trials but has not yet been released in the United States.

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